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Edwin V Merkel Nixon Peabody Clinton Square P O Box 31051 Rochester, NY 14603				EXAMINER MERTZ, PREMA MARIA
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/532,291	KELLY, RODNEY WILLIAM	
	<b>Examiner</b>	<b>Art Unit</b>	
	Prema M. Mertz	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 15 April 2008.

2a) This action is **FINAL**.                            2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1-10, 12-14, 16, 20-45, 47-49, 51, 66, 67, 69, 73-75, 78 and 79 is/are pending in the application.

4a) Of the above claim(s) 3, 4, 20, 21, 27-45, 47-49, 51, 66, 67, 69, 73-75, 78 and 79 is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 1, 2, 5-10, 12-14, 16 and 22-26 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All    b) Some \* c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 9/1/2005.

4) Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.

5) Notice of Informal Patent Application

6) Other: \_\_\_\_\_.

## **DETAILED ACTION**

### ***Election/Restrictions***

1. Applicant's election of Group I (claims 1-2, 5-6, 7-10, 12-14, 16, 22-26, species: (i) Prostaglandin E2 as the prostaglandin which raises the effective cAMP concentration in a monocyte cell; and (ii) "locally at a site where tolerance is required" as the method of administering an agent) with traverse in the reply filed on 4/15/08 is acknowledged. The traversal is on the ground(s) that the restriction is improper because Piquet-Pellorce teaches (in the context of assessing the role of histamine in haematopoiesis) that the combination of PGE2 and GMCSF increases intracellular cAMP and induces histamine synthesis in bone marrow cells, but does not teach or suggest that the combination of PGE2 and GMCSF can be used for inducing tolerance to an antigen, as set forth in claim 1. For these reasons, Applicants argue, unity exists for Groups I-VII, and all claims of Groups I-VII should be examined together. However, contrary to Applicants arguments, while the prior art Piquet-Pellorce disclosure is silent as to the combination of PGE2 and GMCSF can be used for inducing tolerance to an antigen, the instant claims merely recite a newly discovered result, i.e. a method of inducing tolerance to an antigen in a patient by administering the combination of PGE2 and GMCSF. Claim 1 has been interpreted as administering the combination of PGE2 and GMCSF.

Since the first claimed invention of Group I lacks a special technical feature, the other claimed inventions cannot share a special technical feature with the first claimed invention. The inventions of Groups 1-21 are patentably distinct from the products of Groups 22-28 because the products of Groups 22-28 can be used in other methods such as immunoassays or

immunoaffinity chromatography. The methods of Groups 1-21 and 29-32 are patentably distinct from each other because each recites method steps not required by the other, comprise treating different conditions, each method uses different patient populations as starting materials and the search of all methods in one patent application would result in an undue search burden.

The Groups as delineated in the restriction requirement 3/17/2008 are patentably distinct one from the other such that each invention could, by itself, in principle, support its own separate patent (as shown by the arguments put forth in the written restriction requirement).

The requirement is still deemed proper and is therefore made FINAL.

Claims 3-4, 20-21, 27- 45, 47-49, 51, 66-67, 69, 73-75, 78-79 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

***Specification objection***

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below:

The instant application discloses nucleic acid primers on pages 59-65 of the specification. Claim 7 recites SEQ ID NO:2. The application lacks a sequence listing, both paper and CRF. The specification and claims contain nucleic acid sequences and amino acid sequences that require SEQ ID NOs. Applicants submission must include the statement “the sequence listing information recorded in computer readable form is identical to the written (on paper or compact

disc) sequence listing" and, where applicable, includes no new matter, as required by 37 CFR 1.821(e), 1.821(f), 1.821(g), 1.825(b) or 1.825(d).

Correction is required.

***Claim rejections-35 USC § 112, first paragraph, scope of enablement***

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3a. Claims 1-2, 5-10, 12-14, 16, 22-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for inducing tolerance in monocytes by increasing levels of granulysin, CD14, COX-2 and IL-10 and decreasing levels of CIITA and MHCII, the method comprising administering to monocyte cells an effective amount of PGE2 and GM-CSF, does not reasonably provide enablement for a method of inducing tolerance to an antigen in a patient, the method comprising administering to the patient an agent which raises the effective cAMP concentration in a monocyte cell and granulocyte-macrophage colony stimulating factor (GMCSF) or a derivative thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The specification delimits the instant method to administering the antigen HLA-A2 to combat transplant rejection, however, claim 1 for example, recites a method for inducing tolerance to "all" antigens , comprising administering an agent which raises the effective cAMP

concentration in a monocyte cell and granulocyte-macrophage colony stimulating factor (GMCSF) to a patient.

With respect to these claims, as recited, what is claimed in the instant invention broadly encompasses a method of administering "all" agents that raise effective cAMP concentration in a monocyte cell. While the specification, Example 1, page 56, lines 21-26, discloses that:

"There is growing evidence that prostaglandins of the E series are involved in immunological tolerance. This derives from their role in oral tolerance (the ability of the immune system to distinguish pathogenic and commensal organisms), their ability to modulate cytokine ratios, and their huge concentrations in human seminal plasma where tolerance for the spermatozoon is essential."

The results of the experiment demonstrated in Example 1 are shown in Figure 2 and show that there is a synergistic between a prostaglandin (PGE2) and GMCSF on the release of IL-10, CD-14, CD86, COX-2, and granulysin from cells of the immune system (page 62, lines 23-25).

The specification is non-enabling for the unlimited number of compositions comprising "an agent which raises the effective cAMP concentration", and which are encompassed by the scope of the claims. Claim 1, for example, is a single means claim (M.P.E.P. 2164.08(a)). In In re Hyatt, 708 F.2d 712, 218 USPQ 195 (Fed. Cir. 1983), the Courts have held that: "A single means claim, i.e. where a means recitation does not appear in combination with another recited element of means, is subject to an undue breadth rejection under 35 U.S.C. 112, first paragraph." (A single means claim which covered every conceivable means for achieving the stated purpose

was held nonenabling for the scope of the claim because the specification disclosed at most only those means known to the inventor). Since no material limitations for the agent which raises the effective cAMP concentration have been recited in the claim and only a biological activity has been recited, the claim encompasses every conceivable structure (means) for achieving the stated property (result), a fact situation comparable to Hyatt. The claimed invention encompasses a method of administering compositions not envisioned or described in the specification, and neither does the specification disclose how these claimed compositions can be distinguished from each other. The specification only demonstrates (Example 1; Figure 2) that there is a synergism between a prostaglandin (PGE2) and GMCSF on the release of IL-10, CD-14, CD86, COX-2, and granulysin from cells of the immune system (page 62, lines 23-25). These properties of PGE2 may differ structurally, chemically and physically from other known molecules. By application of the factors set forth in Ex parte Forman (230 USPQ 546 (Bd. Pat. App. & Int. 1986), and reiterated in In re Wands (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), which include (1) quantity of experimentation, (2) guidance presented, (3) the predictability of the art, and (4) the breadth of the claims, in the instant application, the quantity of experimentation to determine which other agents to be administered are encompassed by the scope of the claims is practically infinite and the guidance provided in the specification very little, thereby rendering the results of the methods taught in the specification unpredictable (see pages 56-58). Therefore, it would require undue experimentation to determine which agents to be administered in the claimed method would be encompassed by the scope of the claims. The disclosure of PGE2 administration in combination with GM-CSF, is clearly insufficient support

under the first paragraph of 35 U.S.C. § 112 for claims, which encompass every and all agents.

In In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), the Courts have held that:

"Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since some improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that the scope of the claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."

Furthermore, the amount of embodiments corresponding to the desirable compositions in the claimed method, may be innumerable, and the enabled embodiments amount to only one. Therefore, there are substantial scientific reasons to doubt the scope of enablement, as set forth above. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. The specification does not describe inducing tolerance to any other antigen other than HLA-A2 by administering PGE2 and GMCSF, and since it is deemed to constitute undue experimentation to determine all the other agents and antigens, the disclosure is not

commensurate with the scope of the claims. It is suggested that by employing conventional claim language, the claims be amended to include the specific agent and antigen supported by the instant specification in the claimed method.

The claims are drawn very broadly to methods of inducing tolerance to “all” antigens ranging from antigens involved in allergic reactions to antigens involved in autoimmune disease.

Page 25, lines 23-25, of the specification discloses:

“Diseases or conditions where there is an aberrant or undesired immune or inflammatory response may also include allergies, wherein the undesired response is an allergic response. In such a condition or disease, the antigen to which tolerance is induced would be an allergen.”

Page 27, lines 15-30, of the specification discloses:

“In still another embodiment, the invention includes a method of treating an autoimmune disease in a patient, the method comprising administering to the patient an agent which raises the effective cAMP concentration in a monocyte cell and GMCSF. The treatment of an autoimmune disease may involve inducing tolerance to a self-antigen against which there is an undesired immune response.

Autoimmune diseases that may be treated using the methods of the present invention include primary myxoedema, thyrotoxicosis, pernicious anaemia, autoimmune atrophic gastritis, Addison's disease, insulin-dependent diabetes mellitus (IDDM), Goodpasture's syndrome, myasthenia gravis, sympathetic ophthalmia, MS, autoimmune haemolytic anaemia, idiopathic leucopenia, ulcerative colitis, dermatomyositis, scleroderma, mixed connective tissue disease,

rheumatoid arthritis, irritable bowel syndrome, SLE, Hashimoto's disease, thyroiditis, Behcet's disease, coeliac disease/dermatitis herpetiformis, and demyelinating disease."

However, other than inducing tolerance to HLA-A2 antigen effective to combat transplant rejection in a patient, the method comprising administering to the patient an effective amount of PGE2 and GM-CSF (see specification, Example 1, pages 56-62), the specification fails to provide any guidance for the successful induction of tolerance to any other antigens in these other conditions.

The CAFC decision (Genentech Inc. v. Novo Nordisk, 42 USPQ2d 1001, 1997) expressly states that:

"When there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

The treatment of autoimmune disease has been the subject of intense study for the past several decades. Many promising treatments and therapies have been identified via in vitro experiments, and have not lived up to expectations when tested in vivo. In fact, the number of such treatments, which have failed to live up to their promise exceeds those, which have been performed as hoped by orders of magnitude. It would not be reasonable to expect the claimed products to work on the various types of aforementioned autoimmune diseases because it is well

known that results obtained in vitro are generally not reasonably predictive of results to be expected in vivo. Thus, it would require undue experimentation on the part of the skilled artisan to use the claimed method for treated as recited, in the absence of sufficient information to predict the results with an adequate degree of certainty. In view of this unpredictability in the treatment of different autoimmune diseases, there cannot be said to be any reasonable expectation of success at the in vivo application of a potential therapy, especially in view of the fact that the current specification as filed presents no working examples pertaining to the method of treatment of any autoimmune disease in vivo. Given the breadth of claim 1 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of skill in the art to practice the claimed invention.

***Claim rejections-35 USC § 112, first paragraph, written description***

2b. Claims 1-2, 5-10, 12-14, 16, 22-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description in this case only sets forth SEQ ID NO:2 and equivalent degenerative codon sequences thereof and therefore the written description is not commensurate in scope with claim 7 drawn to naturally occurring variants of SEQ ID NO:2.

*Vas-Cath Inc. V. Mahurkar*, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was

in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

Rieger et al (Glossary of Genetics and Cytogenetics, Classical and Molecular, 4th Ed., Springer-Verlay, Berlin, 1976) clearly define alleles as one of two or more alternative forms of a gene occupying the same locus on a particular chromosome..... and differing from other alleles of that locus at one or more mutational sites ( page 17). Thus, the structure of naturally occurring allelic sequences and naturally occurring variants of SEQ ID NO:2 are not defined. With the exception of SEQ ID NO:2, the skilled artisan cannot envision the detailed structure of the encompassed polypeptide and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a

genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

Variants of the disclosed polypeptide may be naturally occurring variants. However, no disclosure, beyond the mere mention of variants is made in the specification (page 12, lines 1-2). This is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Therefore only GMCSF having the amino acid sequence set forth in SEQ ID NO:2 to be used in the claimed method, but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph. As a result, it does not appear that the inventors were in possession of naturally occurring variants of GMCSF of claim 7.

***Claim rejections-35 U.S.C. 112, second paragraph***

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-2, 5-10, 12-14, 16, 22-26, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite for several reasons.

Claim 1, line 1, is vague and indefinite because it recites “an antigen”. The metes and bounds of the claim are unclear because it is unclear which of the numerous antigens known can be used in the claimed method. Appropriate recitation of the antigen for which there is a basis in the instant specification is required

Claim 1 is vague and indefinite because it is a method claim but fails to recite steps in the claim.

Claim 1 is vague and indefinite because it fails to recite the condition that the patient is suffering from.

Claim 1, line 4, is rejected as vague and indefinite because it recites “derivative thereof”. The metes and bounds of this term are unclear.

Claim 2 is vague and indefinite because it recites non-elected species.

Claim 6, line 3, is rejected as vague and indefinite because it recites “analogue thereof”. The metes and bounds of this term are unclear.

Claim 9, line 4, is vague and indefinite because it recites “derivative thereof”. The metes and bounds of this term are unclear.

Claim 16, line 3, is vague and indefinite because it recites “derivative thereof”. The metes and bounds of this term are unclear.

Claim 22, line 3, is vague and indefinite because it recites “derivative thereof”. The metes and bounds of this term are unclear.

Claim 23, line 4, is vague and indefinite because it recites “disease or condition associated with transplant rejection”. The metes and bounds of this term are unclear.

Claim 25, line 3 and line 4, is vague and indefinite because it recites “derivative thereof” with respect to “GMCSF” and “the antigen”. The metes and bounds of this term are unclear in both recitations.

Claims 5, 7-8,10, 12-14, 24, 26 are rejected as vague and indefinite insofar as they depend on the above rejected claim for their limitations.

***Claim Rejections - 35 USC § 103***

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

4a. Claims 1-2, 5-8, 9, 12-14, 16, 22, are rejected under 35 U.S.C. 103(a) as unpatentable over *Piquet-Pellorce et al* (1991) in view in of *Owens et al* (U.S. Patent No. 5,851,784).

Piquet-Pellorce et al teaches a method of administering PGE2 and GMCSF to bone marrow cells to potentiate histamine release and that both PGE2 and GMCSF together increase intracellular cAMP content in a synergistic manner (see abstract; page 2378, last paragraph; page 2379, Figures 1-3; page 2380, first 15 lines). However, the reference does not disclose further administering a phosphodiesterase (PDE) inhibitor in the claimed method.

Owens et al ('784) teaches that intracellular cAMP levels are regulated by degradation by PDE (column 1, lines 9-15) and that PDE IV activity is markedly inhibited by PDE IV selective inhibitors such as rolipram and denbufylline (see column 12, lines 64-67).

Therefore, at the time the invention was made, it would have been *prima facie* obvious to a person of ordinary skill in the art to administer PGE2 and GMCSF as taught by Piquet-Pellorce et al together with a PDE IV inhibitor as taught by Owens et al. The motivation for doing so would have been because Owens teaches that inhibition of PDE activity markedly increases cAMP levels.

With respect to the instant claims, the instantly claimed method has been interpreted as administering only the combination of PGE2 and GMCSF (see claim 1), claim 9 has been interpreted as administering a PDE inhibitor together with PGE2 and GMCSF and claim 22 has been interpreted as administering a PDE inhibitor, PGE2 and GMCSF .

With respect to claim 8, the GMCSF of the prior art would have the same effect as the GMCSF sargramostin recited in instant claim 8 when administered. In the instant case, where the claimed and prior art products to be administered are identical or substantially identical in

structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established.

In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). “When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.” *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the *prima facie* case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433. See also *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985).

Therefore, the method disclosed in the combination of references renders obvious claims 1-2, 5-8, 9, 12-14, 16, and 22.

### ***Double Patenting***

#### ***Non-statutory double patenting rejection (obviousness-type)***

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5a. Claims 1-2, 5-10, 12-14, 16, 22-26 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11, 28-40 of copending Application No. 10/576,437 ('437). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-2, 5-10, 12-14, 16, 22-26 in the instant application claim "a method of inducing tolerance to an antigen in a patient, the method comprising administering to the patient an agent which raises the effective cAMP concentration in a monocyte cell and GMCSF or a derivative thereof". Claims 1-11 and 28-40 of US application '437 (having one common inventor with the instant application), claims "a method of inducing tolerance to a therapeutic cell in a patient who is to be administered subsequently a therapeutic amount of the said therapeutic cell or a precursor thereof, the method comprising administering to the patient (a) a tolerising cell sharing the same antigenic characteristics as the therapeutic cell, or an antigen found thereon or a derivative of said antigen, and (b) an agent which raises the effective cAMP concentration in a monocyte cell". It is clear that the claims differ in scope because the instant claims recite "the method comprising administering" which is open language and encompasses the therapeutic cell administered in the

claims of '437. Therefore, instant claims are generic to the claims in '437 and encompasses subject matter to which claims in '437 are a species. The claims in '437 are obvious from the instant claims because the claims in '437 are directed to a specific embodiment encompassed by the instant claims. The method of '437 is included in instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

### ***Conclusion***

No claim is allowed.

Claims 1-2, 5-10, 12-14, 16, 22-26, are rejected.

### ***Advisory Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835.

Official papers filed by fax should be directed to (571) 273-8300. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Prema Mertz/  
Primary Examiner  
Art Unit 1646

Application/Control Number: 10/532,291  
Art Unit: 1646

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